

REMARKS

Claims 3-15, 18, and 20-21 are now pending in the application. Claims 1-21 are rejected. Claims 1, 2, 16-17, and 19 have been cancelled. New claims 22-24 have been added. Claims 3-7, 9, 11-12, 14, 18, and 20-21 have been amended. Support for the amendments can be found, for example, at page 3, lines 12-14 and line 23 to page 4, line 1, page 14, lines 1-5, page 15, lines 6-8, and page 17, lines 23-26. Claim 9 has been amended to correct a grammatical error. No new matter has been added by way of these amendments.

The pending claims are novel in view of Yu, *et al.*

Claims 1-9, 11-13, and 15 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Yu, H., *et al.* (Journal of Virology, 70:4530-4537 (1996)) (hereinafter "Yu"). To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). Applicants respectfully submit that Yu does not anticipate the claimed invention.

The Office has alleged that Yu anticipates the pending claims because Yu teaches the use of a fusion protein consisting of a tetracycline repressor (tTA) and the activation domain of the herpes simplex virus VP16 domain to regulate transcription of a gene of interest controlled by a minimal cytomegalovirus promoter coupled to tetracycline operator sequences. Unlike the Yu reference, the pending claims recite a packing cell in which the first level of regulation is provided by an inducible promoter selected from the group consisting of a tetracycline promoter/operator, a retroviral long terminal repeat (LTR) and a steroid promoter region. As noted by the Office, Yu does not teach a tetracycline promoter/operator; nor does it teach an inducible LTR or steroid promoter region. Because Yu does not teach all the limitations of the claimed invention, the cited reference does not anticipate the pending claims. As such, Applicants request that the present rejection be withdrawn.

The pending claims are nonobvious over Yu, *et al.* and Ghosh, *et al.*

Claims 1-6, 9, 11-13 and 15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yu, in view of Ghosh, S., *et al.* (J. Mol. Biol., 234:610-619 (1993)) (hereinafter "Ghosh"). To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art reference must teach or suggest all the claim limitations. *See In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Applicants submit that the proposed combination does not support a *prima facie* case of obviousness.

The combination of the Yu and Ghosh references does not render the subject matter of the rejected claims obvious because it does not teach or suggest all the limitations of the pending claims. As previously argued, the subject matter of the presently claimed invention is directed to the use of three constructs that sequentially produce viral gene products encoded by the third construct. The first construct recited in the claims comprises a nucleotide sequence encoding a first inducible promoter and a first product, wherein the first inducible promoter regulates expression of first product and the first inducible promoter is selected from the group consisting of a tetracycline promoter/operator, a retroviral long terminal repeat (LTR), and a steroid promoter region. This arrangement of expression control elements and gene products produced in a cascade-like fashion was designed to permit high levels of viral protein production. The high levels of production are a result of the tight regulation of gene expression produced by the packaging cell lines. Tight regulatory control is desirable where the nucleic acid to be expressed or the level of expression sought is toxic to the host cell (Specification, page 1, lines 9-11).

As discussed above, neither the Yu or Ghosh references teach or suggest the use of a tetracycline promoter/operator or a steroidal promoter. As such, these references fail to render the subject matter of the pending claims obvious. Regarding the Office's allegation that the Ghosh reference renders the use of Tat obvious in the claimed packaging cell line, Applicants respectfully disagree.

Ghosh teaches that Tat and VP16 are both active in regulating transcription from an HIV LTR. However, Ghosh also teaches that Tat functions at only about 1/3 the level of activity as that of VP16 (*see* Ghosh, page 613, Figure 2). Thus, given the markedly reduced activity demonstrated by the substitution of Tat for VP16, one of ordinary skill in the art would not have been motivated to make the substitution proposed by the Office. Reduced promoter activity correlates to reduced protein production. Given the reduction in activity demonstrated by Tat, Applicants submit that Ghosh actually teaches away from using Tat to regulate an HIV LTR, especially when high levels of product are sought. For support of this statement, Applicants respectfully directs the Examiner's attention to the Results section, specifically pages 612 to 613. In view of these observations, Applicants submit that the proposed combination of Ghosh and Yu fails to articulate a *prima facie* case of obviousness. As such, Applicants request that this rejection be withdrawn.

Rejection of claims under 35 U.S.C. § 112, second paragraph

Claims 1-21 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office alleged that the pending claims were indefinite because they recited the phrase "capable of". While respectfully disagreeing with the Office regarding the clarity of this terminology, the pending claims have been amended to omit this phrase.

The Office also alleged that the claims were indefinite because the ordinary artisan would not know what the constructs are or what they look like. Applicant need not and preferably will not disclose that which is already known to one of skill in the art. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 at 1384 (Fed. Cir. 1986). New independent claim 22 contains the subject matter of former independent claim 1, but rewritten to more clearly recite the features of the claimed invention. Each of the three nucleic acid constructs recited in the claim contains an inducible promoter and a gene under the control of that promoter. For example, the first construct can comprise a nucleotide sequence encoding for a tetracycline promoter/operator, a retroviral long

terminal repeat (LTR), or a steroid promoter region. The structures of these inducible promoters are notoriously well known in the art. The second nucleic acid construct encodes a viral RNA binding protein. Again, the structure of a viral RNA binding protein is notoriously well known in the art. Lastly, the third construct comprises a sequence encoding a viral gene product, which is defined, for example, as a viral envelope or G protein, both of these groups of proteins have structures that are notoriously well known in the art.

Because the structure of the genes and the promoters that control them would be recognized by one of ordinary skill in the art as structural features of a nucleic acid, one of skill in the art could readily determine appropriate structures that function within the parameters recited by the pending claims. As such, the pending claims clearly and definitively recite the subject matter of the invention.

Regarding the Office's question as to whether the constructs can be found on the same DNA or if the term nucleic acid construct indicates individual structures, Applicants submit that either of these interpretations fall within the scope of the pending claims. With respect to the Office's allegation that the claims were indefinite because it was not clear whether all the constructs were present in the claimed cell, Applicants submit that the revised wording of claim 22 makes it clear that the claimed cell comprises all three constructs recited in the claim.

Thus, for the reasons discussed above, Applicants submit that the language of independent claim 22 and all claims dependent therefrom are clear and meet the requirements of 35 U.S.C. § 112, second paragraph.

CONCLUSION

The above amendments to the claims are submitted for the purpose of facilitating allowance of the claims and a sincere effort has been made to place this application in condition for allowance. An early notice of allowance is earnestly requested.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (858) 720-7961.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 397272000800. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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